Figure 1A

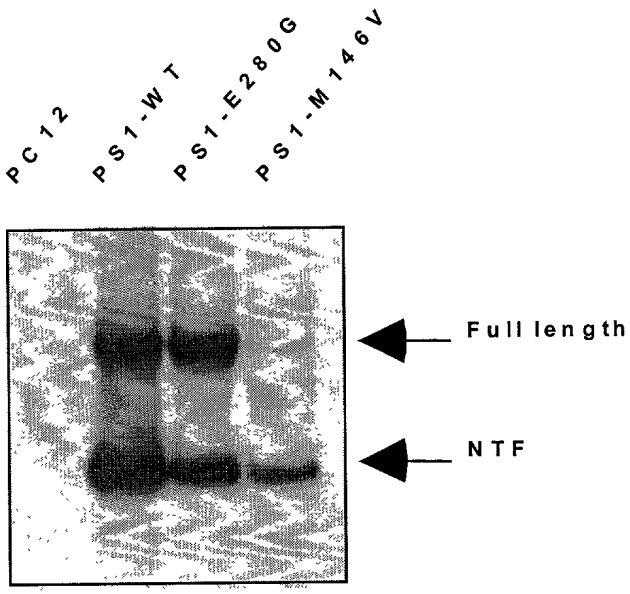


Figure 1B

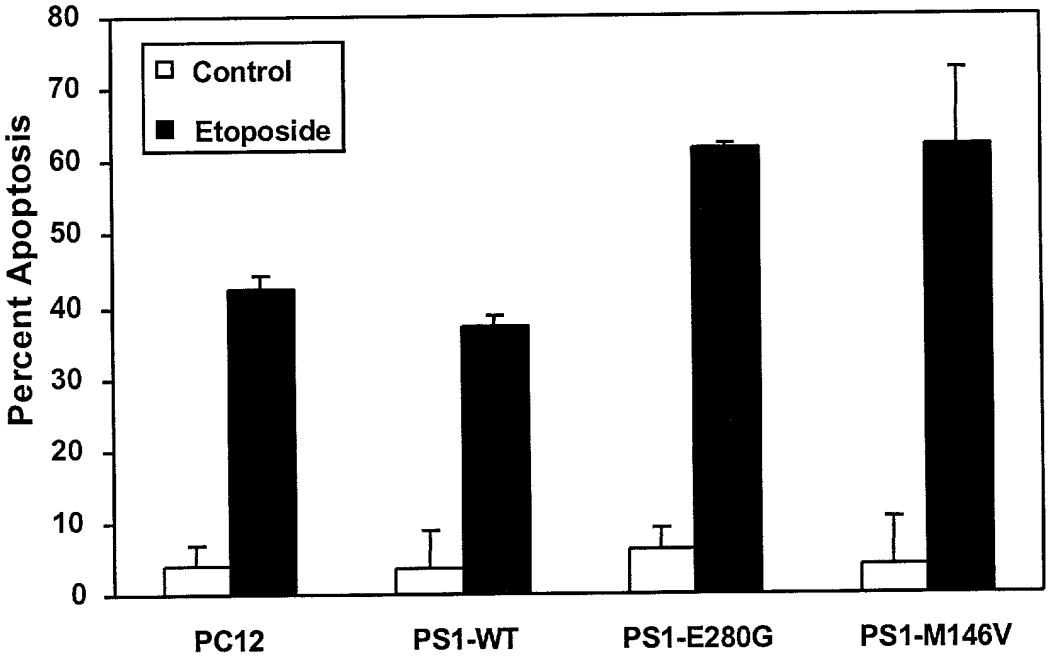

80
70
60
50
40
30
20
10
0
Percent Apoptosis
Control
Etoposide
PC12
PS1-WT
PS1-E280G
PS1-M146V

Figure 1C

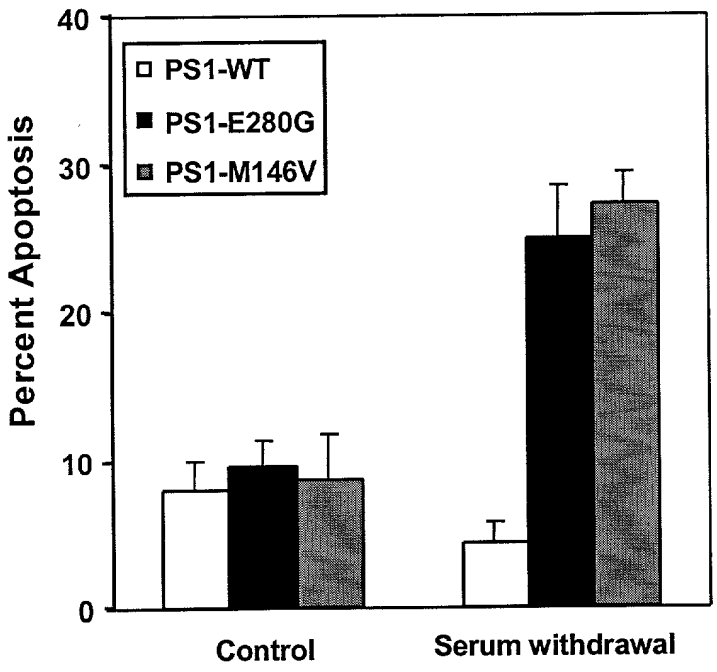

40
30
20
10
0
Percent Apoptosis
PS1-WT
PS1-E280G
PS1-M146V
Control
Serum withdrawal

Figure 1D

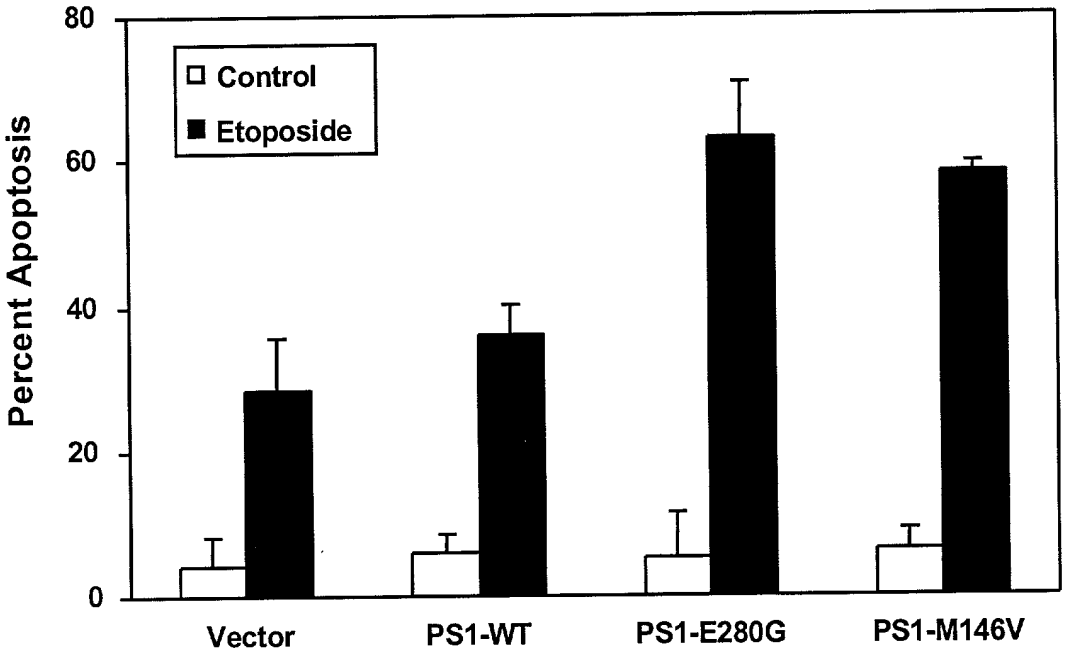

80
60
40
20
0
Percent Apoptosis
Control
Etoposide
Vector
PS1-WT
PS1-E280G
PS1-M146V

Figure 2A

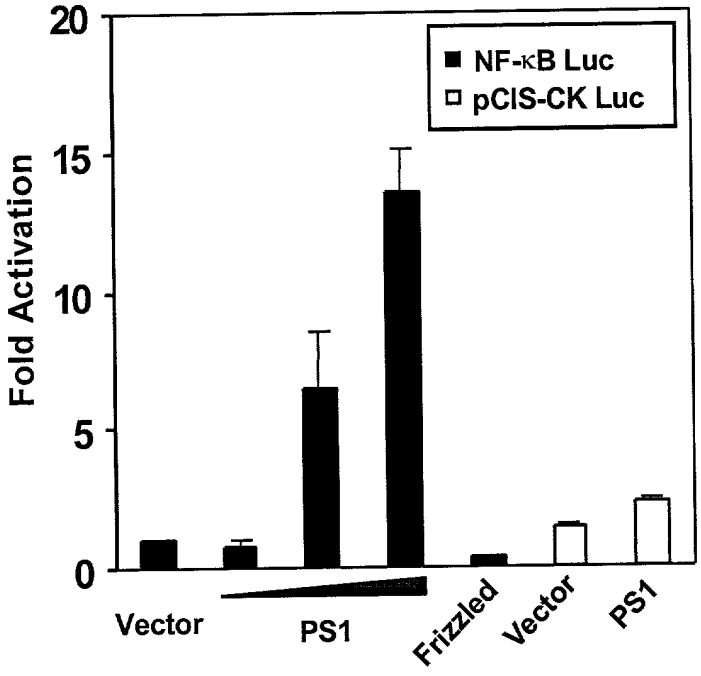

20
15
10
5
0
Fold Activation
NF-κB Luc
pCIS-CK Luc
Vector
PS1
Frizzled
Vector
PS1

Figure 2B

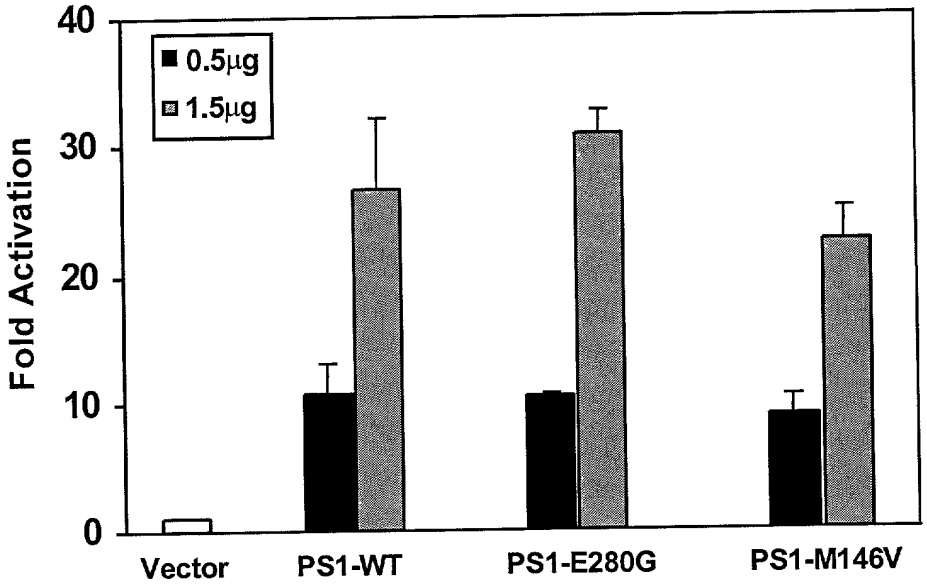

40
30
20
10
0
Fold Activation
0.5μg
1.5μg
Vector
PS1-WT
PS1-E280G
PS1-M146V

Figure 3A

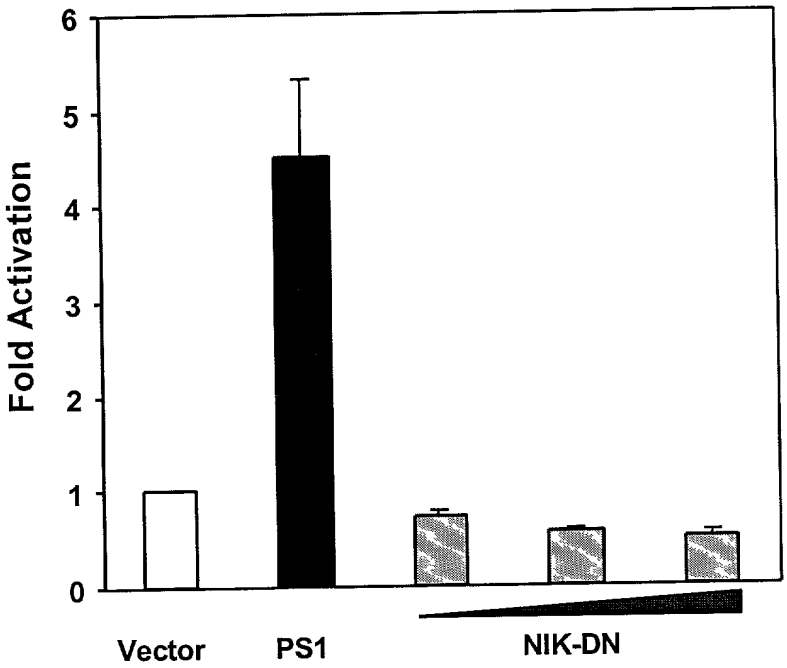


Figure 3B

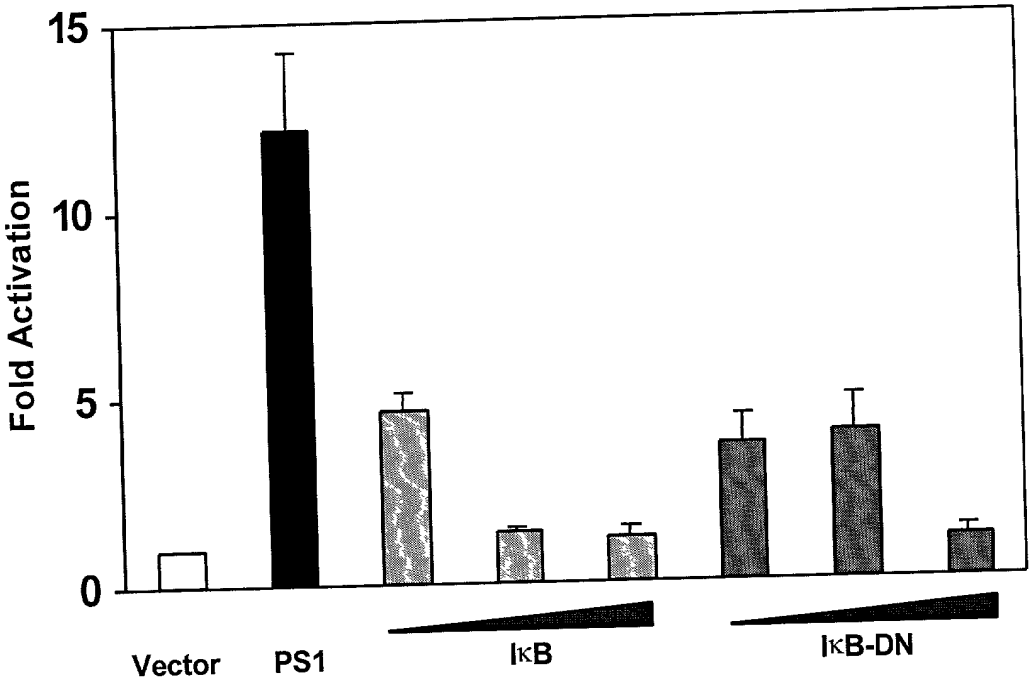


Figure 4A

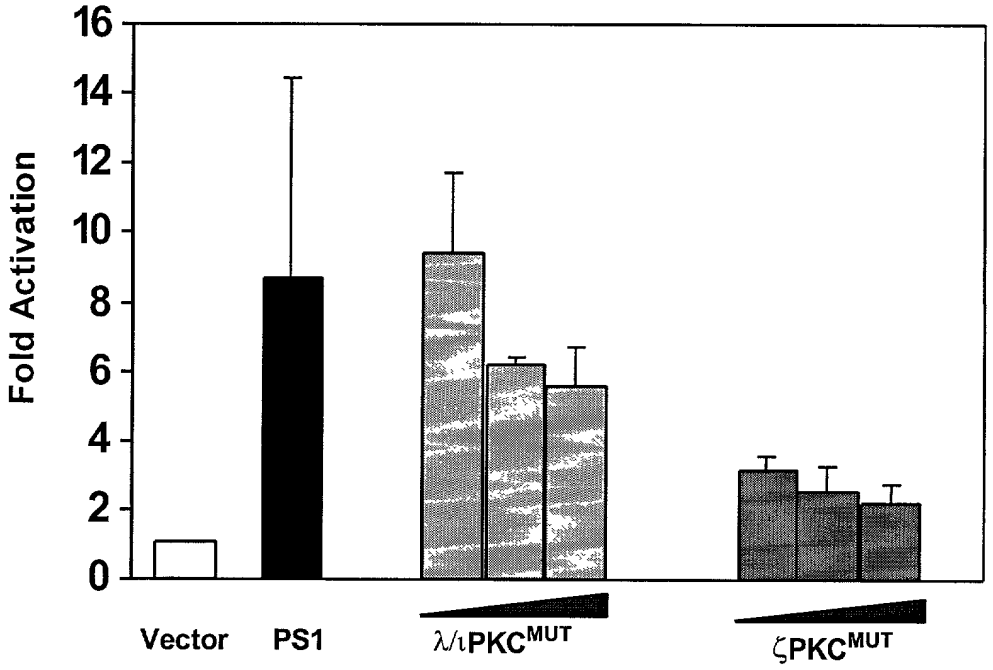

16
14
12
10
8
6
4
2
0
Fold Activation
Vector
PS1
λ/ιPKC^MUT
ζPKC^MUT

Figure 4B

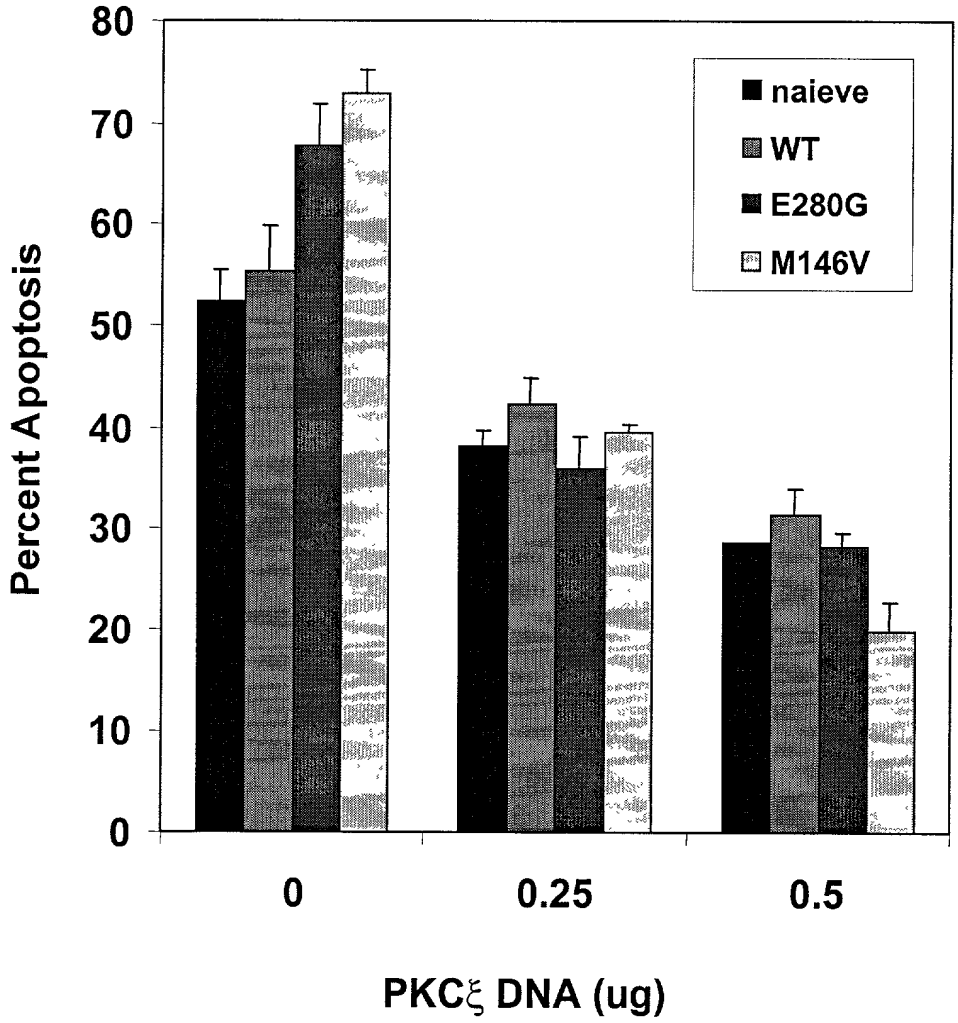

80
70
60
50
40
30
20
10
0
Percent Apoptosis
naieve
WT
E280G
M146V
0
0.25
0.5
PKCξ DNA (ug)

Figure 4C

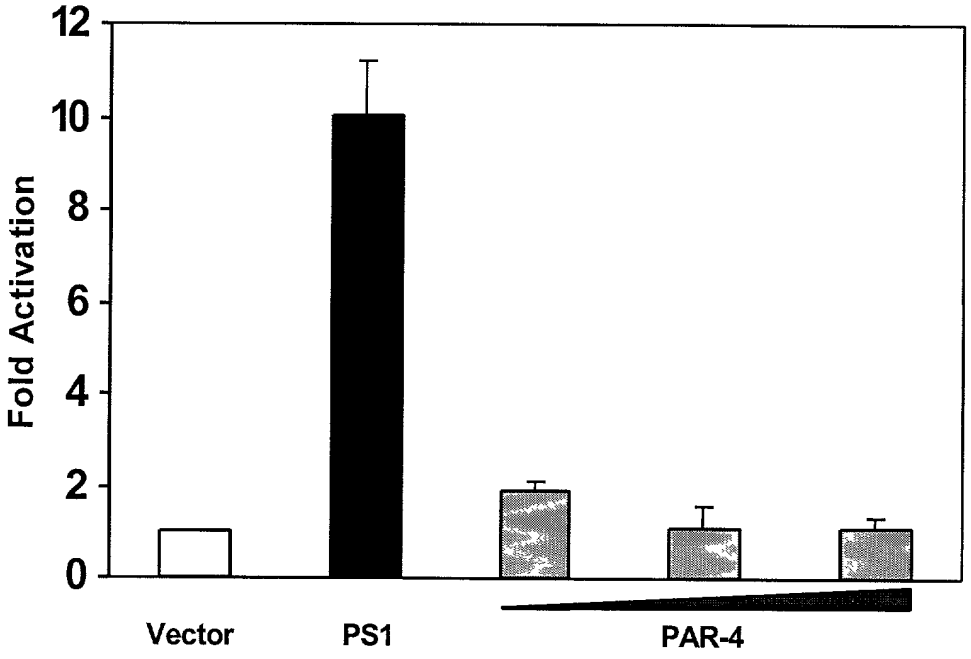


Figure 4D

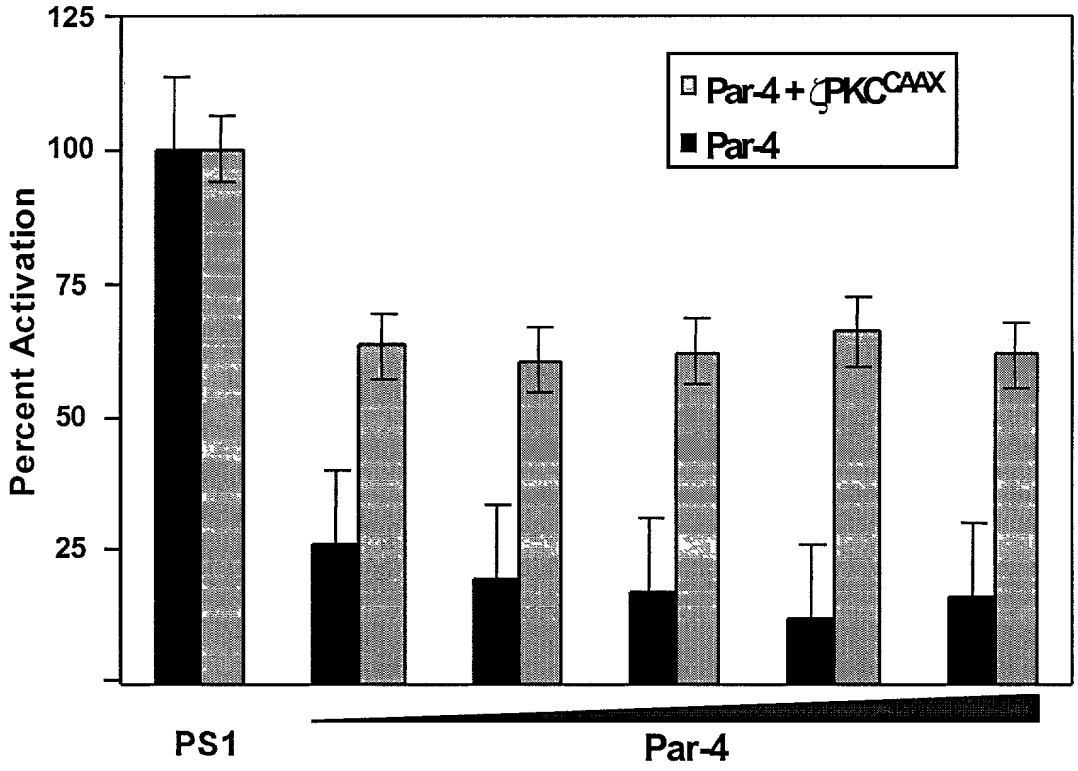

125
100
75
50
25
Percent Activation
Par-4 + ζPKC^CAAX
Par-4
PS1
Par-4

Figure 4E

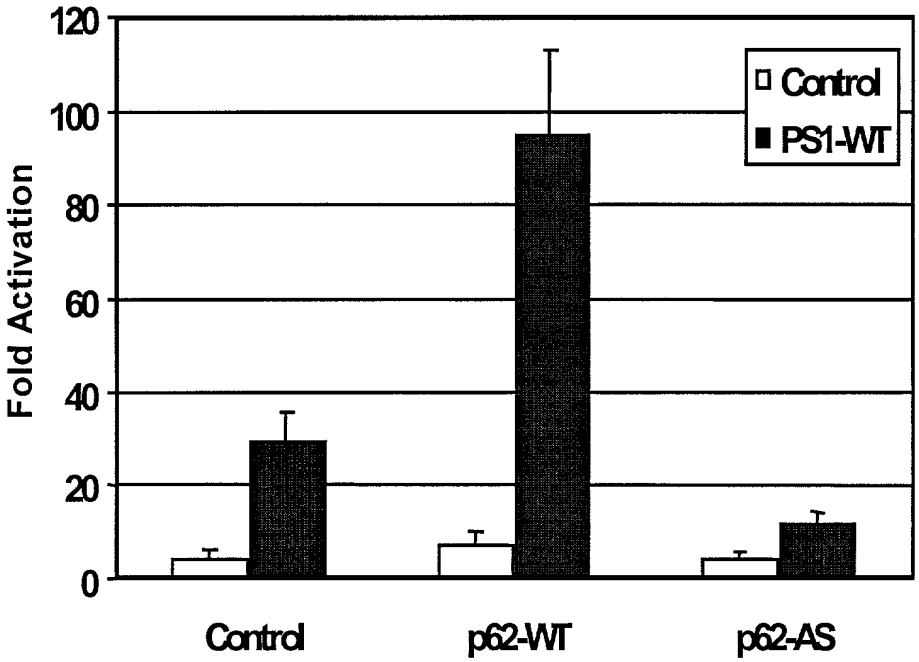

120
100
80
60
40
20
0
Fold Activation
Control
PS1-WT
Control
p62-WT
p62-AS

Figure 5A

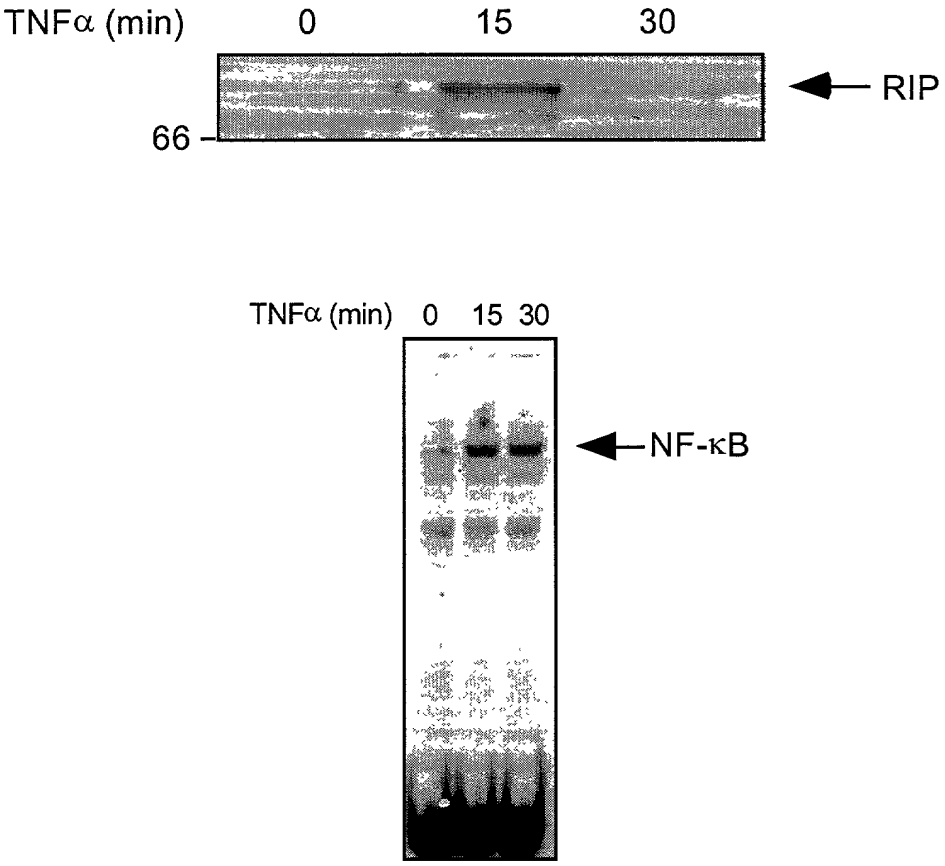


Figure 5B

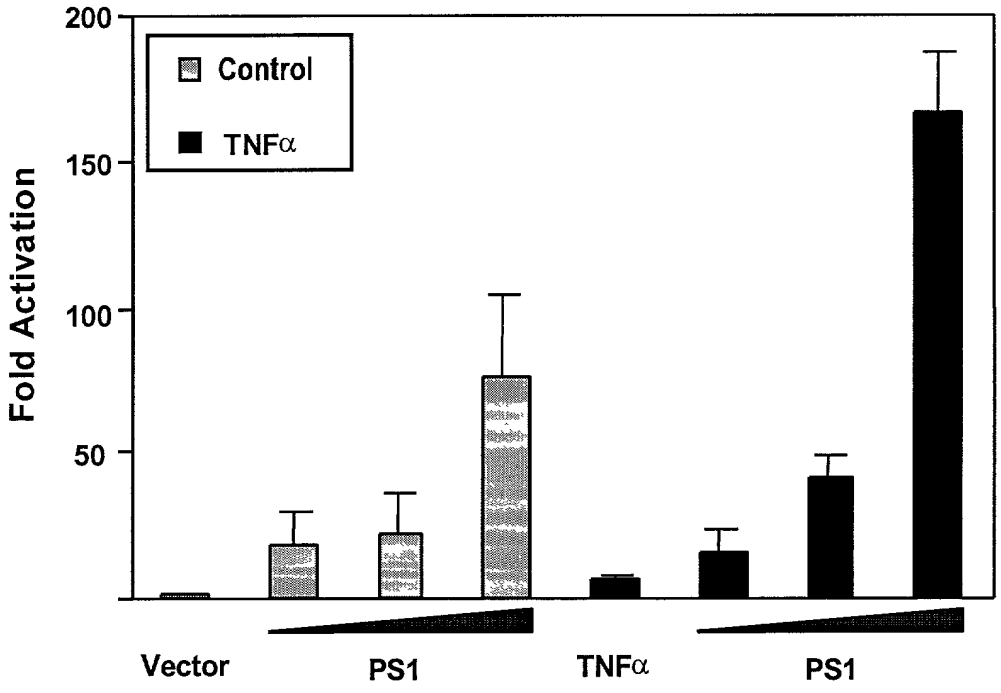

200
150
100
50
Fold Activation
Control
TNFα
Vector
PS1
TNFα
PS1

Figure 5C

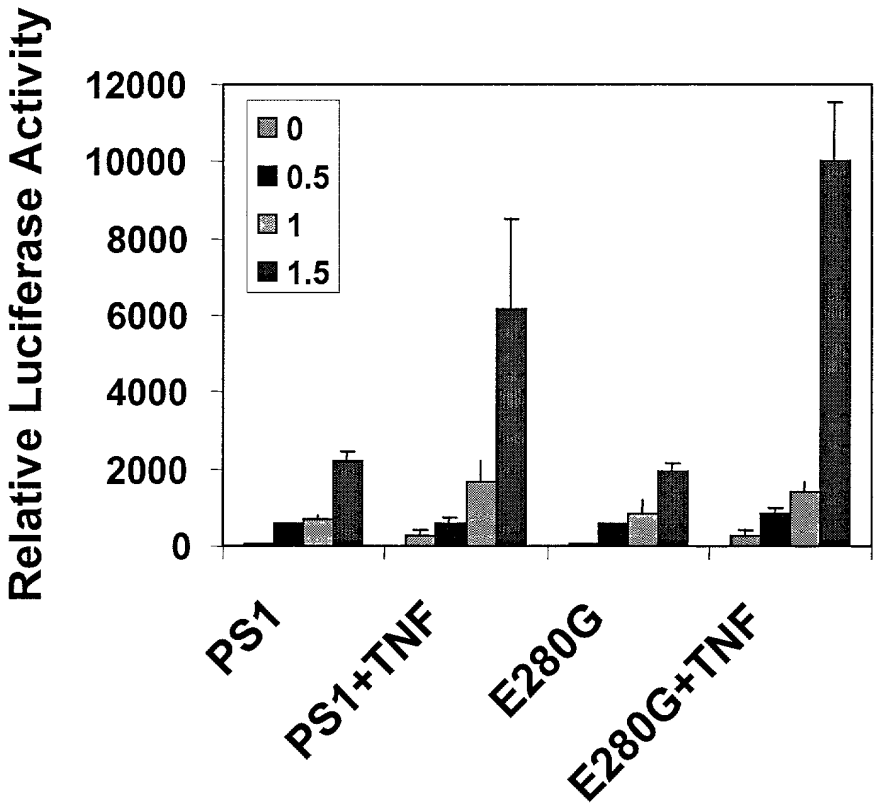

Relative Luciferase Activity
12000
10000
8000
6000
4000
2000
0
0
0.5
1
1.5
PS1
PS1+TNF
E280G
E280G+TNF

Figure 6A

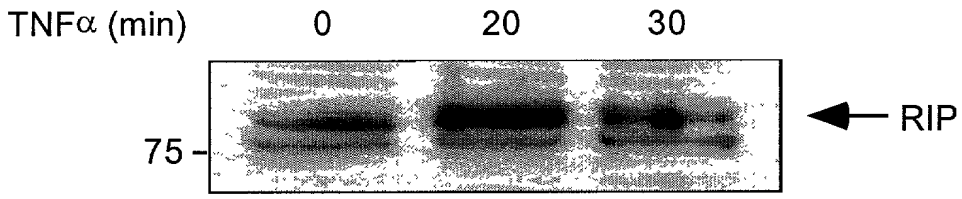


Figure 6B

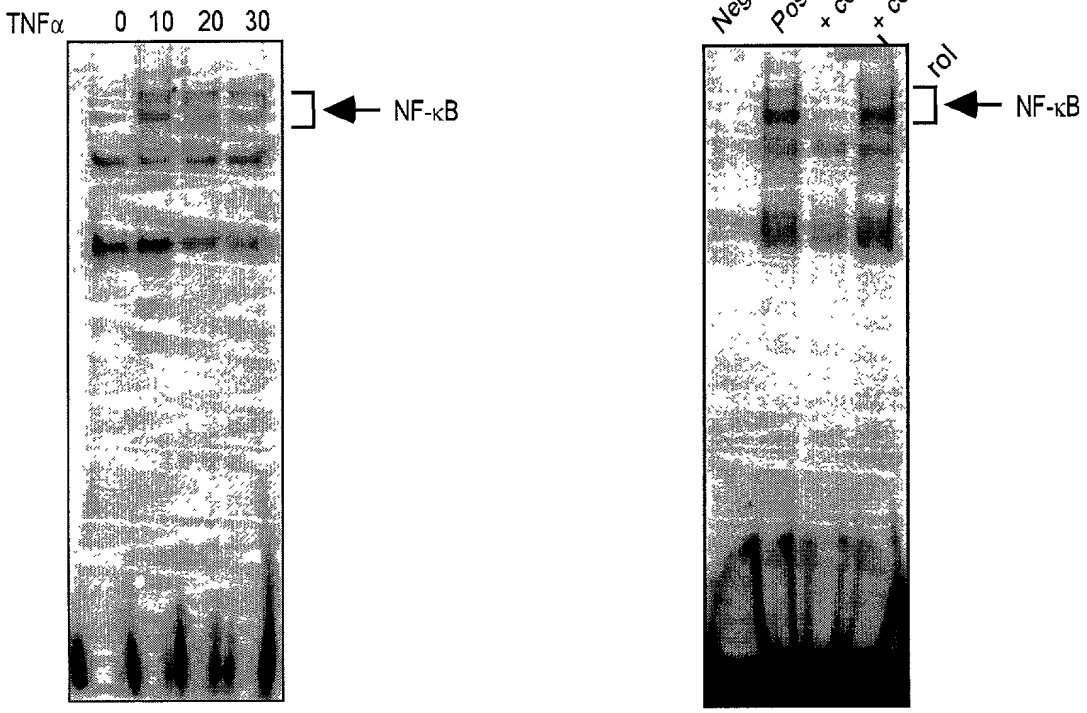

TNFα 0 10 20 30
NF-κB
Negative con
Positive cont
+ cold NF-kB
+ cold SP1
rol
NF-κB

Figure 7A

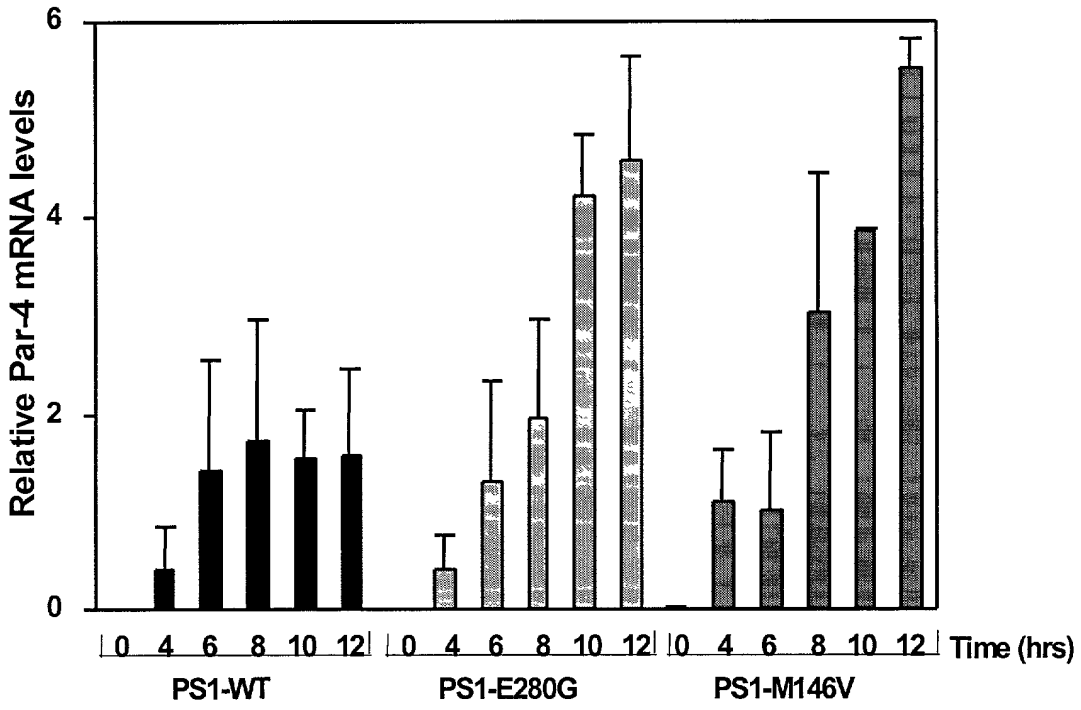

Relative Par-4 mRNA levels
6
4
2
0
0 4 6 8 10 12
0 4 6 8 10 12
0 4 6 8 10 12
Time (hrs)
PS1-WT
PS1-E280G
PS1-M146V

Figure 7B

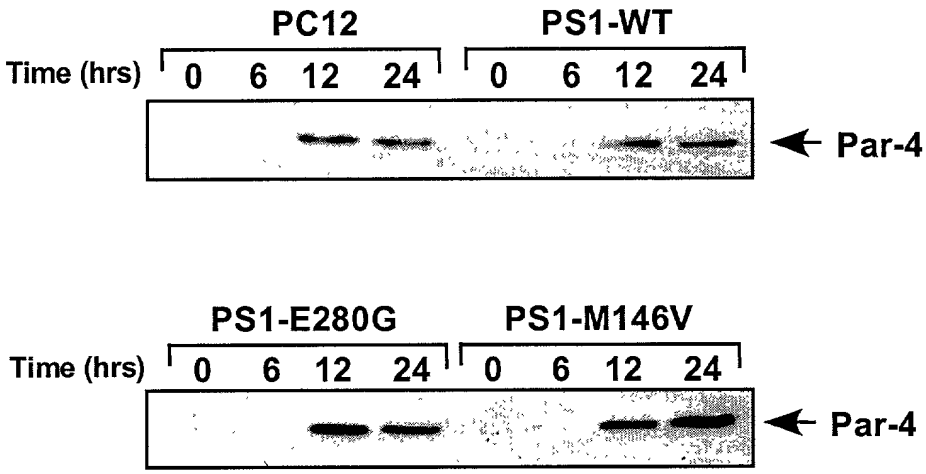
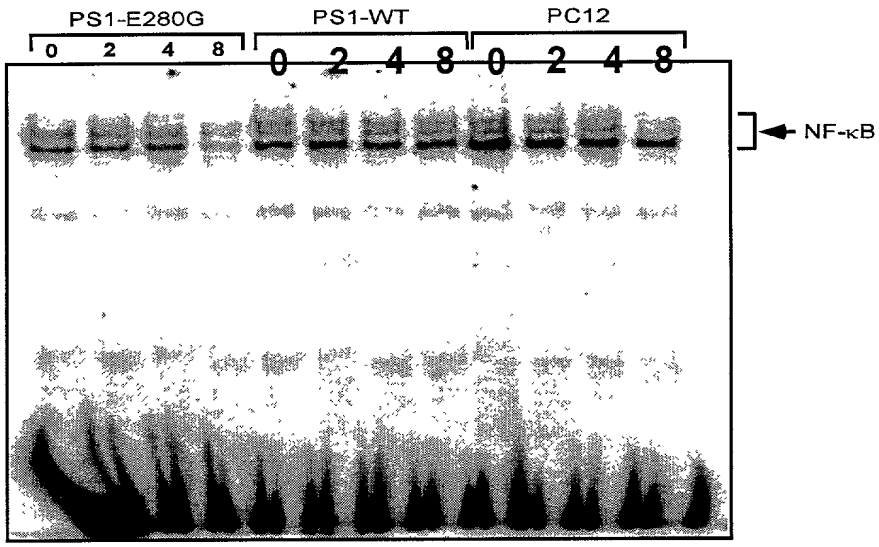

PC12
PS1-WT
Time (hrs)
0 6 12 24
0 6 12 24
Par-4
PS1-E280G
PS1-M146V
Time (hrs)
0 6 12 24
0 6 12 24
Par-4

Figure 8


PS1-E280G
PS1-WT
PC12
0 2 4 8
0 2 4 8 0 2 4 8
NF-κB

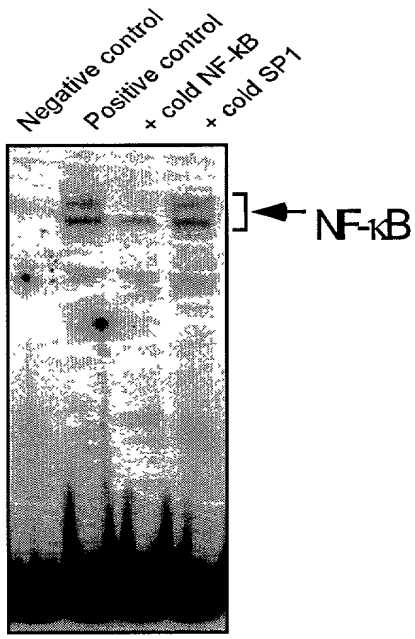

Negative control
Positive control
+ cold NF-kB
+ cold SP1
NF-κB

Figure 9A

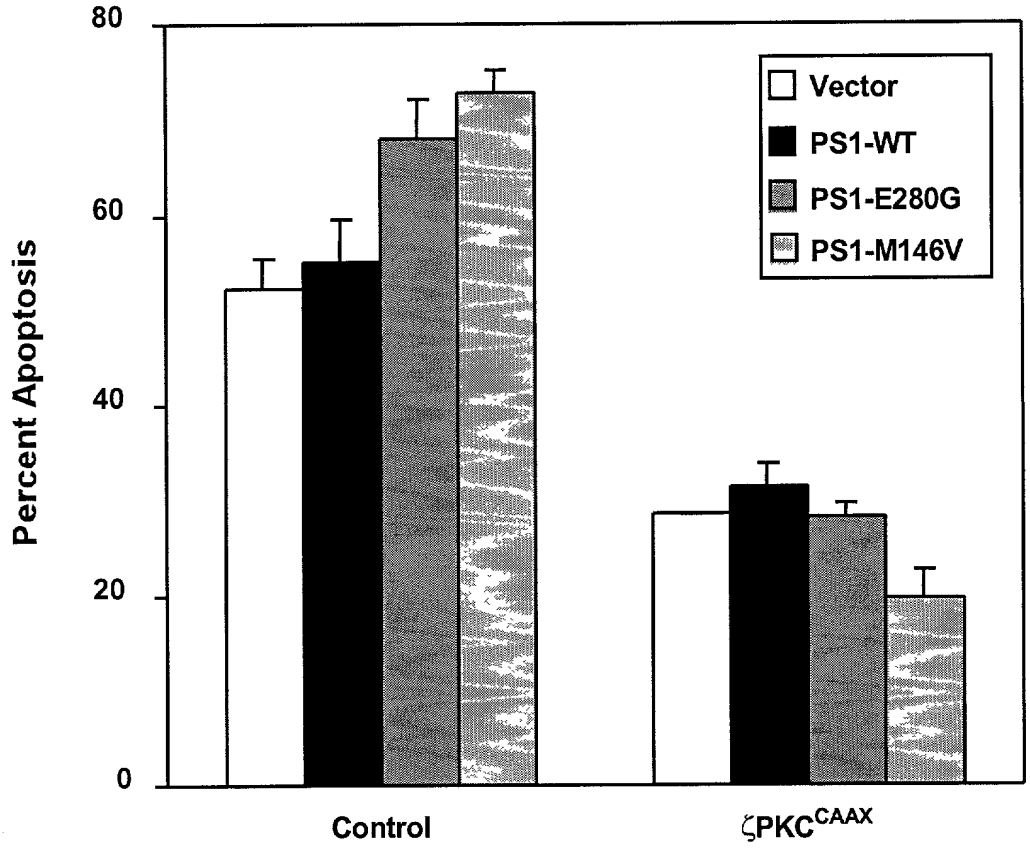

80
60
40
20
0
Percent Apoptosis
Vector
PS1-WT
PS1-E280G
PS1-M146V
Control
ζPKC^CAAX

Figure 9B

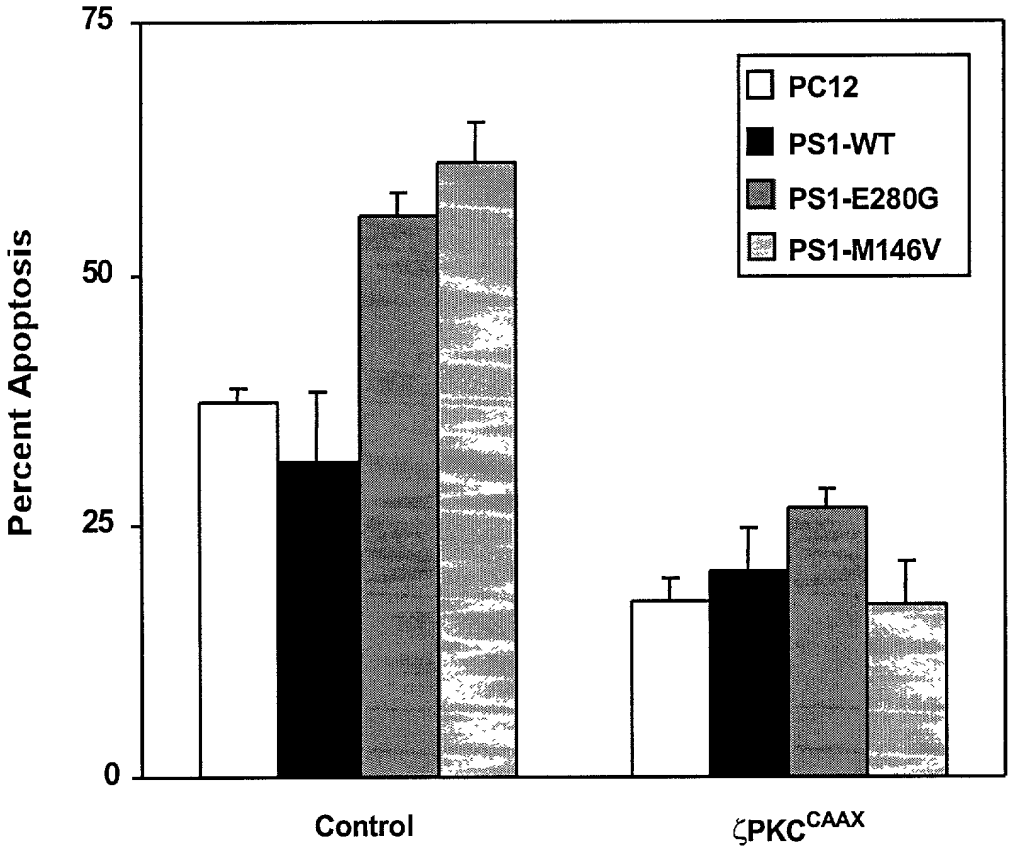

75
50
25
0
Percent Apoptosis
PC12
PS1-WT
PS1-E280G
PS1-M146V
Control
ζPKC^CAAX

Figure 10

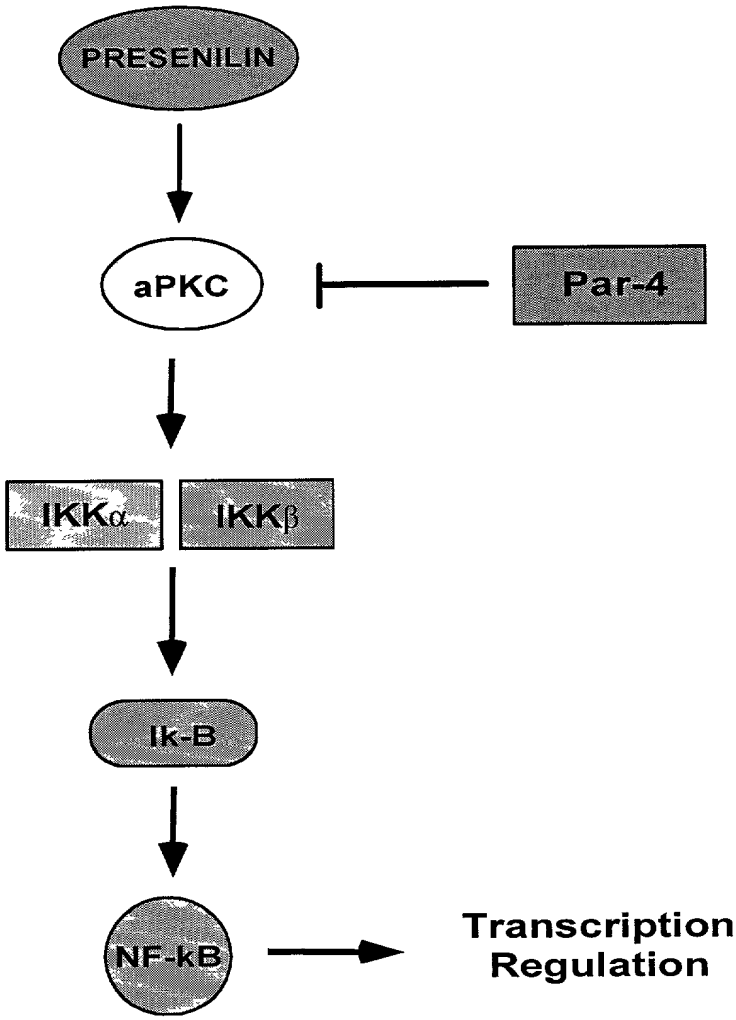

PRESENILIN
aPKC
Par-4
IKKα
IKKβ
Ik-B
NF-kB
Transcription
Regulation

FIGURE 11A

ATGCGCGCCAAGCAGAACCCCCCGGGCCCGGCCCCCCCGGGAGGGGGCAGCAGCGACGCCGC
TGGGAAGCCCCCCGCGGGGGCTCTGGGCACCCCGGCGGCCGCCGCTGCCAACGAGCTCAACA
ACAACCTCCCGGGCGGCGCGCCGGCCGCACCTGCCGTCCCCGGTCCCGGGGGCGTGAACTGC
GCGGTCGGCTCCGCCATGCTGACGCGGGCGCCCCCGGCCCGCGGCCCGCGGCGGTCGGAGGA
CGAGCCCCCAGCCGCCTCTGCCTCGGCTGCACCGCCGCCCCAGCGTGACGAGGAGGAGCCGG
ACGGCGTCCCAGAGAAGGGCAAGAGCTCGGGCCCCAGTGCCAGGAAAGGCAAGGGGCAGATC
GAGAAGAGGAAGCTGCGGGAGAAGCGGCGCTCCACCGGCGTGGTCAACATCCCTGCCGCAGA
GTGCTTAGATGAGTACGAAGATGATGAAGCAGGGCAGAAAGAGCGGAAACGAGAAGATGCAA
TTACACAACAGAACACTATTCAGAATGAAGCTGTAAACTTACTAGATCCAGGCAGTTCCTAT
CTGCTACAGGAGCCACCTAGAACAGTTTCAGGCAGATATAAAAGCACAACCAGTGTCTCTGA
AGAAGATGTCTCAAGTAGATATTCTCGAACAGATAGAAGTGGGTTCCCTAGATATAACAGGG
ATGCAAATGTTTCAGGTACTCTGGTTTCAAGTAGCACACTGGAAAAGAAAATTGAAGATCTT
GAAAAGGAAGTAGTAACAGAAAGACAAGAAAACCTAAGACTTGTGAGACTGATGCAAGATAA
AGAGGAAATGATTGGAAAACTCAAAGAAGAAATTGATTTATTAAATAGAGACCTAGATGACA
TAGAAGATGAAAATGAACAGCTAAAGCAGGAAAATAAAACTCTTTTGAAAGTTGTGGGTCAG
CTGACCAGGTAG

FIGURE 11B

MATGGYRTSSGGGSTTDWKAKRKMRAKNGAGGGSSDAAGKAGAGTAAAAANNNNGGAAAAVG
GGVNCAVGSAMTRAARGRRSDAASASAARDDGVKGKSSGSARKGKGKRKRKRRSTGVVNAAC
DYDDAGKRKRDATNTNAVNDGSSYRTVSGRYKSTTSVSDVSSRYSRTDRSGRYNRDANVSGT
VSSSTKKDKVVTRNRVRMDKMGKKDNRDDDDNKNKTKVVGTRMATGGYRTSSGGGSTTDWKA
KRKMRAKNGAGGGSSDAAGKAGAGTAAAAANNNNGGAAAAVGGGVNCAVGSAMTRAARGRRD
AASASAARDDGVKGKSSGSARKGKGKRKRKR

FIGURE 12A

ATGACAGAGTTACCTGCACCGTTGTCCTACTTCCAGAATGCACAGATGTCTGAG
GACAACCACCTGAGCAATACTGTACGTAGCCAGAATGACAATAGAGAACGGCAG
GAGCACAACGACAGACGGAGCCTTGGCCACCCTGAGCCATTATCTAATGGACGA
CCCCAGGGTAACTCCCGGCAGGTGGTGGAGCAAGATGAGGAAGAAGATGAGGAG
CTGACATTGAAATATGGCGCCAAGCATGTGATCATGCTCTTTGTCCCTGTGACT
CTCTGCATGGTGGTGGTCGTGGCTACCATTAAGTCAGTCAGCTTTTATACCCGG
AAGGATGGGCAGCTAATCTATACCCCATTCACAGAAGATACCGAGACTGTGGGC
CAGAGAGCCCTGCACTCAATTCTGAATGCTGCCATCATGATCAGTGTCATTGTT
GTCATGACTATCCTCCTGGTGGTTCTGTATAAATACAGGTGCTATAAGGTCATC
CATGCCTGGCTTATTATATCATCTCTATTGTTGCTGTTCTTTTTTTCATTCATT
TACTTGGGGGAAGTGTTTAAAACCTATAACGTTGCTGTGGACTACATTACTGTT
GCACTCCTGATCTGGAATTTTGGTGTGGTGGGAATGATTTCCATTCACTGGAAA
GGTCCACTTCGACTCCAGCAGGCATATCTCATTATGATTAGTGCCCTCATGGCC
CTGGTGTTTATCAAGTACCTCCCTGAATGGACTGCGTGGCTCATCTTGGCTGTG
ATTTCAGTATATGATTTAGTGGCTGTTTTGTGTCCGAAAGGTCCACTTCGTATG
CTGGTTGAAACAGCTCAGGAGAGAAATGAAACGCTTTTTCCAGCTCTCATTTAC
TCCTCAACAATGGTGTGGTTGGTGAATATGGCAGAAGGAGACCCGGAAGCTCAA
AGGAGAGTATCCAAAAATTCCAAGTATAATGCAGAAAGCACAGAAAGGGAGTCA
CAAGACACTGTTGCAGAGAATGATGATGGCGGGTTCAGTGAGGAATGGGAAGCC
CAGAGGGACAGTCATCTAGGGCCTCATCGCTCTACACCTGAGTCACGAGCTGCT
GTCCAGGAACTTTCCAGCAGTATCCTCGCTGGTGAAGACCCAGAGGAAAGGGGA
GTAAAACTTGGATTGGGAGATTTCATTTTCTACAGTGTTCTGGTTGGTAAAGCC
TCAGCAACAGCCAGTGGAGACTGGAACACAACCATAGCCTGTTTCGTAGCCATA
TTAATTGGTTTGTGCCTTACATTATTACTCCTTGCCATTTTCAAGAAAGCATTG
CCAGCTCTTCCAATCTCCATCACCTTTGGGCTTGTTTTCTACTTTGCCACAGAT
TATCTTGTACAGCCTTTTATGGACCAATTAGCATTCCATCAATTTTATATCTAG

FIGURE 12B

MTELPAPLSYFQNAQMSEDNHLSNTVRSQNDNRERQEHNDRRSLGHPEPLSNGRPQGNSRQV
VEQDEEEDEELTLKYGAKHVIMLFVPVTLCMVVVVATIKSVSFYTRKDGQLIYTPFTEDTET
VGQRALHSILNAAIMISVIVVMTILLVVLYKYRCYKVIHAWLIISSLLLLFFFSFIYLGEVF
KTYNVAVDYITVALLIWNFGVVGMISIHWKGPLRLQQAYLIMISALMALVFIKYLPEWTAWL
ILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPALIYSSTMVWLVNMAEGDPEAQRRVS
KNSKYNAESTERESQDTVAENDDGGFSEEWEAQRDSHLGPHRSTPESRAAVQELSSSILAGE
DPEERGVKLGLGDFIFYSVLVGKASATASGDWNTTIACFVAILIGLCLTLLLLAIFKKALPA
LPISITFGLVFYFATDYLVQPFMDQLAFHQFYI

FIGURE 13A

ATGCTCACATTCATGGCCTCTGACAGCGAGGAAGAAGTGTGTGATGAGCGGACGTCCCTAAT
GTCGGCCGAGAGCCCCACGCCGCGCTCCTGCCAGGAGGGCAGGCAGGGCCCAGAGGATGGAG
AGAACACTGCCCAGTGGAGAAGCCAGGAGAACGAGGAGGACGGTGAGGAGGACCCTGACCGC
TATGTCTGTAGTGGGGTTCCCGGGCGGCCGCCAGGCCTGGAGGAAGAGCTGACCCTCAAATA
CGGAGCGAAGCACGTGATCATGCTGTTTGTGCCTGTCACTCTGTGCATGATCGTGGTGGTAG
CCACCATCAAGTCTGTGCGCTTCTACACAGAGAAGAATGGACAGCTCATCTACACGACATTC
ACTGAGGACACACCCTCGGTGGGCCAGCGCCTCCTCAACTCCGTGCTGAACACCCTCATCAT
GATCAGCGTCATCGTGGTTATGACCATCTTCTTGGTGGTGCTCTACAAGTACCGCTGCTACA
AGTTCATCCATGGCTGGTTGATCATGTCTTCACTGATGCTGCTGTTCCTCTTCACCTATATC
TACCTTGGGGAAGTGCTCAAGACCTACAATGTGGCCATGGACTACCCCACCCTCTTGCTGAC
TGTCTGGAACTTCGGGGCAGTGGGCATGGTGTGCATCCACTGGAAGGGCCCTCTGGTGCTGC
AGCAGGCCTACCTCATCATGATCAGTGCGCTCATGGCCCTAGTGTTCATCAAGTACCTCCCA
GAGTGGTCCGCGTGGGTCATCCTGGGCGCCATCTCTGTGTATGATCTCGTGGCTGTGCTGTG
TCCCAAAGGGCCTCTGAGAATGCTGGTAGAAACTGCCCAGGAGAGAAATGAGCCCATATTCC
CTGCCCTGATATACTCATCTGCCATGGTGTGGACGGTTGGCATGGCGAAGCTGGACCCCTCC
TCTCAGGGTGCCCTCCAGCTCCCCTACGACCCGGAGATGGAAGAAGACTCCTATGACAGTTT
TGGGGAGCCTTCATACCCCGAAGTCTTTGAGCCTCCCTTGACTGGCTACCCAGGGGAGGGCT
GGAGGAAGAGGAGGAAAGGGGCGTGAAGCTTGGCCTCGGGGACTTCATCTTCTACAGTGTGC
TGGTGGGCAAGGCGGCTGCCACGGGCAGCGGGGACTGGAATACCACGCTGGCCTGCTTCGTG
GCCATCCTCATTGGCTTGTGTCTGACCCTCCTGCTGCTTGCTGTGTTCAAGAAGGCGCTGCC
CGCCCTCCCCATCTCCATCACGTTCGGGCTCATCTTTTACTTCTCCACGGACAACCTGGTGC
GGCCGTTCATGGACACCCTGGCCTCCCATCAGCTCTACATCTGA

FIGURE 13B

MLTFMASDSEEEVCDERTSLMSAESPTPRSCQEGRQGPEDGENTAQWRSQENEEDGEEDPDR
YVCSGVPGRPPGLEEELTLKYGAKHVIMLFVPVTLCMIVVVATIKSVRFYTEKNGQLIYTTF
TEDTPSVGQRLLNSVLNTLIMISVIVVMTIFLVVLYKYRCYKFIHGWLIMSSLMLLFLFTYI
YLGEVLKTYNVAMDYPTLLLTVWNFGAVGMVCIHWKGPLVLQQAYLIMISALMALVFIKYLP
EWSAWVILGAISVYDLVAVLCPKGPLRMLVETAQERNEPIFPALIYSSAMVWTVGMAKLDPS
SQGALQLPYDPEMEEDSYDSFGEPSYPEVFEPPLTGYPGEELEEEEERGVKLGLGDFIFYSV
LVGKAAATGSGDWNTTLACFVAILIGLCLTLLLLAVFKKALPALPISITFGLIFYFSTDNLV
RPFMDTLASHQLYI

FIGURE 14

GAATTCGGCACGAGGGGCGCCGCTCGGCTCCCTTCCCGCCCCTGGCTCCCTCCCTCCCTCCCTC
CCTCCTTCTTCTCCCTCCCTCCTGTCCTGGGATTGCCTGGAGCTCCGCACCGCGAGTTTGCCGC
GGCACTTTCCGCGCGGCGGAAGAGCGCGCGCCAGCTTCGGCACACCTGGGAGCCGGATCCCAGC
CCTACGCCTCGTCCCCTACAAGCTCCTCCAAGCCCCGCCGGCTGCTGTGGGAGCGGCGGCCGTC
CCTCTCCTGGAGGTCGTCTCCTGGCATCCTCGGGGCCGCAGGAAGGAAGAGGAGGCAGCGGCCG
GAGCCCTGGTGGGCGGCCTGAGGTGAGAGCCCGACCGGCCCCTTTGGGAAT

FIGURE 15

GAATTCCAGAAGGCAGGAACAGAGAAAGTAGAAGGAAAGTCTTATAAAAGAAAGAGAATAGGCC
AGGCACGGTGGCTCACGCCTCTAATCCCAGCATTTTGGGAGGCTGAGGCAGGTGGATCATGAGG
TCAGGAGTTCAAGACCAACCTGACCAACATGGTGAAGCCCCGTCTCTACTAAAAATACAAAAAT
TAACCAGGCGTGTGTGCCTGTAATCCCAGCTACTCAGGAGGCTGAGGCAGGAGAATCGCTTGAA
CCCGAAAGGTGAAGGTTGCTGTGAGCCTAGATCAGGCCACTGCACTCTGACCTGGGCGACAGAG
CGAGACTCCATGTCAAAGAAAAAGAAAGAGGATAAGAAAATTTCCTAACTGGAAGGCAGATAGC
TGATTAAAAGGGTCCACTGACTGCATAACATAATAATGATAAAAGACCAAATCAGAGCATATCT
TCAAGATATTTCAGAGGATCTAAGTAAGAAGATCCAAAAATTTTGAGACAGAAAATACAATGCA
ATCAGAATGCCACTGGTCTTCTAAACAGCAACTCTGGAAACTAGATGATAATAAAGCAATGCCT
TCAAAATTATGAAGGAAAATGCTTTCTAACCTAGAGTTCTATGCTCCACCAAACTATTAATCAA
GTATGAAGATAAATTTAAAACATTTTCCAATATGCAAGGTCTCTAAGAATGAGTTATACTATCT
TCAGAATATACTGAGGATATACTCTGCTAAAATGAAGGGGAGAAACAAAAAGAGAAAAGTATGC
AATTCAGGAAACAAGAAGTCTACAGAGAAAATGATTCTCAAGGTGTTAGAGGAGCATAATCCCA
GGATGACCACAAGCAACGAGCCTTAAAATCAGTCCAGATTAGGCCAGGTGCGGTGGCTCACACC
TGTAATCCCAGCACTTTGGGAGGCCAAAGCAGGCTGGTTGCCTGAGCTCAGAAGTTCGAGACCA
GTCTGGGCAACATGGTGAAACCCCCGTCTCTACTAAAATACAAAAAATTAGCTGGGCGTGGTGG
CATGTGCCTGTATTCCCAGCTACTCTGGAGGCTGATGCAGGAGAATTGCTTGAACCCAGGAGGC
GGAGGTTGCAGTGAGCCAAGACTGCGCCACTGCACTACAGCCTCACCAACAGAGCGAGACTCCG
TCTCCAAACAAACAAACAAAATCAATCCATATTAAAGCAGGGGATGGAGGGCTCCAGAACAGAT
GTTTCCAAAAAGAGAATAGAACTGATAGCTTACCCAATGTGATTAACGTCATTGAGAGGAGGAA
AATTTGAGTATATACTTGTGACTGGTATATAAAAAAATAAGCCGATGATTAAAGAAAAAAAAAG
AGGCAAGTTTTAACTGCAGAAAAATGGTAAAGACAAAAGGTATAGTTGTGCAACAAGGAAAAAC
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